oculopharyngeal muscular dystrophy

Oculopharyngeal muscular dystrophy is a genetic condition characterized by muscle weakness that begins in adulthood, typically after age 40. The first symptom in people with this disorder is usually droopy eyelids (ptosis), followed by difficulty swallowing (dysphagia). The swallowing difficulties begin with food, but as the condition progresses, liquids can be difficult to swallow as well. Many people with this condition have weakness and wasting (atrophy) of the tongue. These problems with food intake may cause malnutrition. Some affected individuals also have weakness in other facial muscles.

Individuals with oculopharyngeal muscular dystrophy frequently have weakness in the muscles near the center of the body (proximal muscles), particularly muscles in the upper legs and hips. The weakness progresses slowly over time, and people may need the aid of a cane or a walker. Rarely, affected individuals need wheelchair assistance.

There are two types of oculopharyngeal muscular dystrophy, which are distinguished by their pattern of inheritance. They are known as the autosomal dominant and autosomal recessive types.

Frequency

In Europe, the prevalence of oculopharyngeal muscular dystrophy is estimated to be 1 in 100,000 people. The autosomal dominant form of this condition is much more common in the French-Canadian population of the Canadian province of Quebec, where it is estimated to affect 1 in 1,000 individuals. Autosomal dominant oculopharyngeal muscular dystrophy is also seen more frequently in the Bukharan (Central Asian) Jewish population of Israel, affecting 1 in 600 people.

The autosomal recessive form of this condition is very rare; only a few cases of autosomal recessive oculopharyngeal muscular dystrophy have been identified.

Genetic Changes

Mutations in the *PABPN1* gene cause oculopharyngeal muscular dystrophy. The *PABPN1* gene provides instructions for making a protein that is active (expressed) throughout the body. In cells, the PABPN1 protein plays an important role in processing molecules called messenger RNAs (mRNAs), which serve as genetic blueprints for making proteins. The protein alters a region at the end of the mRNA molecule that protects the mRNA from being broken down and allows it to move within the cell.

The PABPN1 protein contains an area where the protein building block (amino acid) alanine is repeated 10 times. This stretch of alanines is known as a polyalanine tract. The role of the polyalanine tract in normal PABPN1 protein function is unknown.

Mutations in the *PABPN1* gene that cause oculopharyngeal muscular dystrophy result in a PABPN1 protein that has an extended polyalanine tract. The extra alanines cause the PABPN1 protein to form clumps within muscle cells that accumulate because they cannot be broken down. These clumps (called intranuclear inclusions) are thought to impair the normal functioning of muscle cells and eventually cause cell death. The progressive loss of muscle cells most likely causes the muscle weakness seen in people with oculopharyngeal muscular dystrophy. It is not known why dysfunctional PABPN1 proteins seem to affect only certain muscle cells.

Inheritance Pattern

Most cases of oculopharyngeal muscular dystrophy are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. People with autosomal dominant oculopharyngeal muscular dystrophy have a mutation resulting in a PABPN1 protein with an expanded polyalanine tract of between 12 and 17 alanines.

Less commonly, oculopharyngeal muscular dystrophy can be inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. In autosomal recessive oculopharyngeal muscular dystrophy, *PABPN1* mutations lead to a polyalanine tract that is 11 alanines long. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Muscular Dystrophy, Oculopharyngeal
- Oculopharyngeal dystrophy
- OPMD
- Progressive muscular dystrophy, oculopharyngeal type

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Oculopharyngeal muscular dystrophy https://www.ncbi.nlm.nih.gov/gtr/conditions/C0270952/

Other Diagnosis and Management Resources

- GeneReview: Oculopharyngeal Muscular Dystrophy
  https://www.ncbi.nlm.nih.gov/books/NBK1126
- MedlinePlus Encyclopedia: Ptosis
  https://medlineplus.gov/ency/article/001018.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Ptosis
  https://medlineplus.gov/ency/article/001018.htm
- Health Topic: Muscular Dystrophy
  https://medlineplus.gov/musculardystrophy.html
- Health Topic: Swallowing Disorders
  https://medlineplus.gov/swallowingdisorders.html

Genetic and Rare Diseases Information Center

- Oculopharyngeal muscular dystrophy
  https://rarediseases.info.nih.gov/diseases/7245/oculopharyngeal-muscular-dystrophy

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Muscular Dystrophy
  https://www.ninds.nih.gov/Disorders/All-Disorders/Muscular-Dystrophy-Information-Page
- National Institute of Neurological Disorders and Stroke: Swallowing Disorders
  https://www.ninds.nih.gov/Disorders/All-Disorders/Swallowing-disorders-Information-Page
- National Institute on Deafness and Other Communication Disorders: Dysphagia
  https://www.nidcd.nih.gov/health/dysphagia

Educational Resources

- Disease InfoSearch: Oculopharyngeal muscular dystrophy
  http://www.diseaseinfosearch.org/Oculopharyngeal+muscular+dystrophy/5329
- MalaCards: oculopharyngeal muscular dystrophy
  http://www.malacards.org/card/oculopharyngeal_muscular_dystrophy
- Orphanet: Oculopharyngeal muscular dystrophy
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=270
- Washington Univeristy, St. Louis: Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/musdist/peeom.html#opd

Patient Support and Advocacy Resources

- Muscular Dystrophy Association
  https://www.mda.org/disease/oculopharyngeal-muscular-dystrophy
- Muscular Dystrophy Canada
  http://www.muscle.ca/about-muscular-dystrophy/types-of-neuromuscular-disorders/oculopharyngeal-muscular-dystrophy/
- Muscular Dystrophy UK: Muscular Dystrophies
  http://www.musculardystrophyuk.org/about-muscle-wasting-conditions/muscular-dystrophies/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/oculopharyngeal-muscular-dystrophy/
- University of Kansas Medical Center Resource List
  http://www.kumc.edu/gec/support/muscular.html

GeneReviews

- Oculopharyngeal Muscular Dystrophy
  https://www.ncbi.nlm.nih.gov/books/NBK1126

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22oculopharyngeal+muscular+dystrophy%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28oculopharyngeal+muscular+dystrophy%5BTIAB%5D%29+OR+%28OPMD%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- OCULOPHARYNGEAL MUSCULAR DYSTROPHY
  http://omim.org/entry/164300

Sources for This Summary

- Abu-Baker A, Rouleau GA. Oculopharyngeal muscular dystrophy: recent advances in the understanding of the molecular pathogenic mechanisms and treatment strategies. Biochim Biophys Acta. 2007 Feb;1772(2):173-85. Epub 2006 Oct 11. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17110089
- Brais B. Oculopharyngeal muscular dystrophy: a late-onset polyalanine disease. Cytogenet Genome Res. 2003;100(1-4):252-60. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14526187
- Müller T, Deschauer M, Kolbe-Fehr F, Zierz S. Genetic heterogeneity in 30 German patients with oculopharyngeal muscular dystrophy. J Neurol. 2006 Jul;253(7):892-5. Epub 2006 Apr 20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16619122
- Robinson DO, Hammans SR, Read SP, Sillibourne J. Oculopharyngeal muscular dystrophy (OPMD): analysis of the PABPN1 gene expansion sequence in 86 patients reveals 13 different expansion types and further evidence for unequal recombination as the mutational mechanism. Hum Genet. 2005 Mar;116(4):267-71. Epub 2005 Jan 12.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15645184
- Robinson DO, Wills AJ, Hammans SR, Read SP, Sillibourne J. Oculopharyngeal muscular dystrophy: a point mutation which mimics the effect of the PABPN1 gene triplet repeat expansion mutation. J Med Genet. 2006 May;43(5):e23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16648376
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2564528/
- Rüegg S, Lehky Hagen M, Hohl U, Kappos L, Fuhr P, Plasilov M, Müller H, Heinimann K. Oculopharyngeal muscular dystrophy - an under-diagnosed disorder? Swiss Med Wkly. 2005 Oct 1; 135(39-40):574-86. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16333769
- Semmler A, Kress W, Vielhaber S, Schröder R, Kornblum C. Variability of the recessive oculopharyngeal muscular dystrophy phenotype. Muscle Nerve. 2007 May;35(5):681-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17206657

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/oculopharyngeal-muscular-dystrophy

Reviewed: December 2008
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services